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Patent
Attorney's Docket No. AMI-009-RC2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
Thomas E. JENKINS, et al.)
Application No.: 10/075,017) Group Art Unit: 1627
Filed: February 13, 2002) Examiner: Unassigned
For: NOVEL THERAPEUTIC AGENTS FOR)
MEMBRANE TRANSPORTERS)

**REPLY TO NOTICE TO FILE CORRECTED APPLICATION PAPERS
and
PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This reply is being submitted in response to the Notice to File Corrected Application Papers mailed on April 4, 2002, for the above-identified patent application. This notice set a two-month period for response, so this reply is due on or before June 4, 2002.

Additionally, Applicants respectfully request entry of the following preliminary amendments prior to examination of this application on the merits:

In the Claims:

Please delete Claim 37, without prejudice or disclaimer, and add in place thereof, the following new claims:

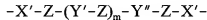
64. (Newly Added) A method of preparing a library of compounds of the formula:



wherein

each L is independently a ligand which binds to a cell membrane transporter; and

X is a linker of the formula:



wherein

m is an integer of from 0 to 20;

X' at each separate occurrence is selected from the group consisting of -O-, -S-, -NH-, -C(O)-, -C(O)O-, -C(O)NH- and a covalent bond;

Z at each separate occurrence is selected from the group consisting of alkylene, cycloalkylene, alkenylene, alkynylene, arylene, heteroarylene, heterocyclene and a covalent bond;

Y' and Y'' at each separate occurrence are selected from the group consisting of -C(O)NR'-, -NR'C(O)-, -NR'C(O)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -NR'-C(O)-O-, -P(O)(OR')-O-, -S(O)_nCR'R'', -S(O)_n-NR'-, -S-S- and a covalent bond; where n is 0, 1 or 2; and

R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic;

the method comprising the steps of:

(a) identifying a ligand compound which binds to a cell membrane transporter;

(b) providing a plurality of functionalized ligand compounds, each functionalized ligand compound comprising the ligand compound from step (a) having a reactive functional group selected from the group consisting of an $-\text{NH}_2$, $-\text{COOH}$, $-\text{C}(\text{O})\text{Y}$, $-\text{CHO}$, $-\text{OH}$, $-\text{SH}$, $-\text{N}=\text{C}=\text{O}$ and $-\text{Y}$ group, where Y is halo; wherein the reactive functional group of each functionalized ligand compound is located at a different position relative to the other functionalized ligand compounds;

(c) providing a linker compound comprising two reactive functional groups independently selected from the group consisting of an $-\text{NH}_2$, $-\text{COOH}$, $-\text{C}(\text{O})\text{Y}$, $-\text{CHO}$, $-\text{OH}$, $-\text{SH}$, $-\text{N}=\text{C}=\text{O}$ and $-\text{Y}$ group, where Y is halo; wherein each of the reactive function groups of the linker compound has complementary reactivity to the reactive functional group of a functionalized ligand compound from step (b);

(d) reacting the linker compound from step (c) with each of the functionalized ligand compounds from step (b) to provide a library of compounds of the formula $\text{L}-\text{X}-\text{L}$.

65. (Newly Added) The method of Claim 64, wherein the method further comprises the step of:

(e) assaying each compound of the library from step (d) to determine its affinity for the cell membrane transporter.

66. (Newly Added) The method of Claim 64, wherein the linker compound has a chain length between reactive functional groups of from about 2 Å to 100 Å.

67. (Newly Added) The method of Claim 64, wherein the cell membrane transporter is an ion channel.

68. (Newly Added) The method of Claim 67, wherein the cell membrane transporter is a sodium ion channel.

REMARKS

Entry of the above amendments and consideration of the following remarks is respectfully requested.

1. **Status of the Claims**

Claims 1-36 and 38-63 were cancelled in the Preliminary Amendment submitted with this application on its filing date, i.e., February 13, 2002. In the above amendments, remaining Claim 37 has been cancelled and Claims 64-68 have been substituted in place thereof. Accordingly, Claims 64-68 are pending for examination on the merits.

2. **Summary of the Amendments**

Initially, Applicants note that a Preliminary Amendment was filed with this application on its filing date, i.e. February 13, 2002. In this amendment, the specification was amended to include further information on related applications and Claims 1-36 and 38-63 were cancelled.

In the present amendments, remaining Claim 37 has been cancelled without prejudice or disclaimer. Applicants specifically reserve the right to pursue the subject matter of this cancelled claim in a continuation application.

New Claims 64-68 have been added. Support for these newly added claims is found, for example, in the following locations of the application as originally filed:

For Claim 64: On page 12, line 24 to page 13, line 28; page 57, lines 12-14; page 58, line 19 to page 59, line 11; and page 80, line 01 to page 89, line 14.

For Claim 65: On page 44, lines 13-16; page 86, line 21 to page 87, line 08; and Table 3 on pages 217 and 218.

For Claim 66: On page 16, lines 7-8; and page 43, lines 10-12.

For Claim 67: On page 36, lines 23-26.

For Claim 68: On page 72, lines 22-23.

Entry of the above amendments is respectfully requested.

3. Substitute Specification

A Notice to File Corrected Application Papers was mailed on April 4, 2002, for this application indicating that a substitute specification was required in compliance with 37 C.F.R. §1.52 because the submitted papers allegedly contained improper margins. (A copy of this Notice is enclosed.)

In response, a substitute specification is submitted herewith in which each sheet of the specification has a left margin of at least 2.5 cm and top, bottom and right margins of at least 2.0 cm.

The table found on pages 90-95 of the specification has been redrawn for increased legibility and reproducibility. Additional pages have been numbered as 90a-f, 91a-e, 92a-c, 93a-e, 94a-c, and 95.

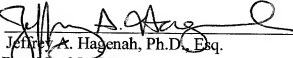
4. Information Disclosure Statement

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicants enclose an Information Disclosure Statement and a modified form PTO-1449 listing documents for consideration by the Examiner. Applicants respectfully request that an Examiner initialed copy of this form be returned to the undersigned.

Accordingly, Applicants believe this application is now ready for examination on the merits and early examination is respectfully requested. Should there be any questions concerning this response, the undersigned Attorney for Applicants can be reached at (650) 808-6406.

Respectfully submitted,
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(formerly ADVANCED MEDICINE, INC.)

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